

- (a) an amino acid sequence sharing at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
  - (b) an amino acid sequence having greater than 60% amino acid identity with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
  - (c) an amino acid sequence defined by Generic Sequences 1, 2, 3, 4, 5 or 6 (SEQ ID NOs: 1, 2, 3, 4, 30 or 31), or
  - (d) an amino acid sequence defined by OPX (SEQ ID NO: 29),
- by:
- (1) providing a candidate compound;
  - (2) determining the expression level of said morphogen in a cell before and after contacting said cell with said candidate compound;

C1 wherein said candidate compound is identified as said agent if there is an increase in the expression level of said morphogen in said cell after contacting said cell with said candidate compound, when compared to the expression level of said morphogen in said cell before contacting said cell with said candidate compound,

- (ii) administering one or more agents identified in step (i) to said mammal, thereby alleviating tissue destructive effects associated with an inflammatory response to an injured tissue in a mammal.

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23. (Amended Twice) A method for reducing tissue damage associated with ischemia-reperfusion injury in a human, the method comprising:

- C2
- (i) identifying one or more agents that stimulates *in vivo* a therapeutically effective concentration of an endogenous morphogen having an amino acid sequence selected from at least one of:
    - (a) an amino acid sequence sharing at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,

- (b) an amino acid sequence having greater than 60% amino acid identity with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
- (c) an amino acid sequence defined by Generic Sequences 1, 2, 3, 4, 5 or 6 (SEQ ID NOs: 1, 2, 3, 4, 30 or 31), or
- (d) an amino acid sequence defined by OPX (SEQ ID NO: 29),

by:

- (1) providing a candidate compound;
- (2) determining the expression level of said morphogen in a cell before and after contacting said cell with said candidate compound;

c<sup>2</sup>  
wherein said candidate compound is identified as said agent if there is an increase in the expression level of said morphogen in said cell after contacting said cell with said candidate compound, when compared to the expression level of said morphogen in said cell before contacting said cell with said candidate compound,

- (ii) administering to said human one or more agents identified in step (i), thereby providing to said injured tissue a therapeutically effective concentration of said morphogen sufficient to alleviate the damage associated with said injury.

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49. (Amended Twice) A method for reducing tissue damage associated with hyperoxia injury in a human, the method comprising:

- (i) identifying one or more agents that stimulates *in vivo* a therapeutically effective concentration of an endogenous morphogen having an amino acid sequence selected from at least one of:
  - (a) an amino acid sequence sharing at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
  - (b) an amino acid sequence having greater than 60% amino acid identity with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,

(c) an amino acid sequence defined by Generic Sequences 1, 2, 3, 4, 5 or 6 (SEQ ID NOs: 1, 2, 3, 4, 30 or 31), or

(d) an amino acid sequence defined by OPX (SEQ ID NO: 29),

by:

(1) providing a candidate compound;

(2) determining the expression level of said morphogen in a cell before and after contacting said cell with said candidate compound;

wherein said candidate compound is identified as said agent if there is an increase in the expression level of said morphogen in said cell after contacting said cell with said candidate compound, when compared to the expression level of said morphogen in said cell before contacting said cell with said candidate compound,

(ii) administering to said human one or more agents identified in step (i), thereby providing to said injured tissue a therapeutically effective concentration of said morphogen sufficient to alleviate the damage associated with said injury.

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50. **(Reiterated)** The method of claim 3, wherein the tissue destructive effects associated with an inflammatory response are the result of a chronic or acute inflammatory disease.

51. **(Reiterated)** The method of claim 3, wherein the tissue destructive effects associated with an inflammatory response are the result of an autoimmune disease.

52. **(Reiterated)** The method of claim 50, wherein the chronic or acute inflammatory disease comprises a disease of joints.

53. **(Reiterated)** The method of claim 52, wherein the disease of the joints is selected from osteoarthritis or rheumatoid arthritis.

54. **(Reiterated)** The method of claim 50, wherein the chronic or acute inflammatory disease comprises a lung disease.

55. **(Reiterated)** The method of claim 54, wherein the lung disease is selected from at least one of bronchitis, emphysema, idiopathic pulmonary fibrosis, adult respiratory distress disorder, or asthma.
56. **(Reiterated)** The method of claim 50, wherein the chronic or acute inflammatory disease comprises a kidney disease.
57. **(Reiterated)** The method of claim 56, wherein the kidney disease is glomular nephritis.
58. **(Reiterated)** The method of claim 50, wherein the chronic or acute inflammatory disease comprises a skin disease.
59. **(Reiterated)** The method of claim 58, wherein the skin disease is selected from psoriasis or dermatitis.
60. **(Reiterated)** The method of claim 50, wherein the chronic or acute inflammatory disease comprises a disorder of gastrointestinal mucosa.
61. **(Reiterated)** The method of claim 60, wherein the disorder of gastrointestinal mucosa is an inflammatory bowel disease or oral mucositis.
62. **(Reiterated)** The method of claim 61, wherein the inflammatory bowel disease is selected from at least one of ulcerative colitis, ileitis, Crohn's disease, or proctitis.
63. **(Reiterated)** The method of claim 50, wherein the chronic or acute inflammatory disease comprises a vascular disease.
64. **(Reiterated)** The method of claim 63, wherein the vascular disease is atherosclerosis or vasculitis.
65. **(Reiterated)** The method of claim 51, wherein the autoimmune disease is selected from diabetes or multiple sclerosis.
66. **(Reiterated)** The method of claim 23, wherein administering said agent is conducted after onset of ischemia but before reperfusion.

67. **(Reiterated)** The method of claim 23, wherein administering said agent is conducted before onset of ischemia.
68. **(Reiterated)** The method of claim 23, wherein said injured tissue is selected from at least one of lung tissue, neural tissue, cardiac tissue, or renal tissue.
69. **(Reiterated)** The method of claim 23, wherein said ischemia-reperfusion injury is associated with a condition selected from at least one of cardiac arrest, pulmonary embolism, renal arterial occlusion, coronary artery occlusion, myocardial infarction, occlusive stroke, cerebral embolism, or asphyxiation.
70. **(Reiterated)** The method of claim 23 or 49, wherein said tissue damage is associated with a tissue graft or organ transplant.

Please add the following new claims.

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71. **(New)** The method of claim 3, 23, or 49, wherein said cell is from a cell type that produces measurable level of said morphogen.
72. **(New)** The method of claim 3, 23, or 49, wherein said cell originates from the same type of tissue as said injured tissue.
- c4. 73. **(New)** The method of claim 3, 23, or 49, wherein said cell is cultured *in vitro*.
74. **(New)** The method of claim 3, 23, or 49, wherein the expression level of said morphogen is determined by the abundance of mRNA or protein of said morphogen.
75. **(New)** The method of claim 74, wherein the abundance of mRNA or protein of said morphogen is measured from: lysate of said cell, culture supernatant of said cell, or a portion of an *in vitro* culture of said cell, with or without radio-isotope labeling.
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<p><i>The claims presented above incorporate changes as indicated by the marked-up versions below.</i></p>
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3. (Amended Twice) A method for alleviating tissue destructive effects associated with an inflammatory response to an injured tissue in a mammal, comprising:

- (i) ~~identifying one or more agents administering to said mammal an agent~~ that stimulates *in vivo* a therapeutically effective concentration of an endogenous morphogen having an amino acid sequence selected from at least one of:
- (a) an amino acid sequence sharing at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
  - (b) an amino acid sequence having greater than 60% amino acid identity with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
  - (c) an amino acid sequence defined by Generic Sequences 1, 2, 3, 4, 5 or 6 (SEQ ID NOs: 1, 2, 3, 4, 30 or 31), or
  - (d) an amino acid sequence defined by OPX (SEQ ID NO: 29),
- by:
- (1) providing a candidate compound;
  - (2) determining the expression level of said morphogen in a cell before and after contacting said cell with said candidate compound;
- wherein said candidate compound is identified as said agent if there is an increase in the expression level of said morphogen in said cell after contacting said cell with said candidate compound, when compared to the expression level of said morphogen in said cell before contacting said cell with said candidate compound.
- (ii) administering one or more agents identified in step (i) to said mammal, thereby alleviating tissue destructive effects associated with an inflammatory response to an injured tissue in a mammal.

23. (Amended Twice) A method for reducing tissue damage associated with ischemia-reperfusion injury in a human, the method comprising:

(i) ~~identifying one or more agents the step of providing to an injured tissue a therapeutic concentration of a morphogen sufficient to alleviate the damage associated with said injury, wherein said step of providing a therapeutically effective morphogen concentration to said injured tissue comprises administering to said human an agent that stimulates *in vivo* a therapeutically effective concentration of an endogenous morphogen having an amino acid sequence selected from at least one of:~~

- (a) an amino acid sequence sharing at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
- (b) an amino acid sequence having greater than 60% amino acid identity with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
- (c) an amino acid sequence defined by Generic Sequences 1, 2, 3, 4, 5 or 6 (SEQ ID NOs: 1, 2, 3, 4, 30 or 31), or
- (d) an amino acid sequence defined by OPX (SEQ ID NO: 29),

by:

- (1) providing a candidate compound;
- (2) determining the expression level of said morphogen in a cell before and after contacting said cell with said candidate compound;

wherein said candidate compound is identified as said agent if there is an increase in the expression level of said morphogen in said cell after contacting said cell with said candidate compound, when compared to the expression level of said morphogen in said cell before contacting said cell with said candidate compound,

(ii) administering to said human one or more agents identified in step (i), thereby providing to said injured tissue a therapeutically effective concentration of said morphogen sufficient to alleviate the damage associated with said injury.

49. (Amended Twice) A method for reducing tissue damage associated with hyperoxia injury in a human, the method comprising:

~~(i) identifying one or more agents the step of providing to an injured tissue a therapeutic concentration of a morphogen sufficient to alleviate the damage associated with said injury, wherein said step of providing a therapeutically effective morphogen concentration to said injured tissue comprises administering to said human an agent that stimulates *in vivo* a therapeutically effective concentration of an endogenous morphogen having an amino acid sequence selected from at least one of:~~

- (a) an amino acid sequence sharing at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
- (b) an amino acid sequence having greater than 60% amino acid identity with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 38-139 of SEQ ID NO: 5,
- (c) an amino acid sequence defined by Generic Sequences 1, 2, 3, 4, 5 or 6 (SEQ ID NOs: 1, 2, 3, 4, 30 or 31), or
- (d) an amino acid sequence defined by OPX (SEQ ID NO: 29),

by:

(1) providing a candidate compound;

(2) determining the expression level of said morphogen in a cell before and after contacting said cell with said candidate compound;

wherein said candidate compound is identified as said agent if there is an increase in the expression level of said morphogen in said cell after contacting said cell with said candidate compound, when compared to the expression level of said morphogen in said cell before contacting said cell with said candidate compound,